

(FILE 'HOME' ENTERED AT 16:03:13 ON 05 DEC 2003)

FILE 'REGISTRY' ENTERED AT 16:03:27 ON 05 DEC 2003

L1 STRUCTURE UPLOADED
L2 11 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 16:04:13 ON 05 DEC 2003

L3 30 S L2
L4 14 S L2/USES OR L2/BIOL
L5 0 S L4 AND HAIR
L6 0 S L4 AND THYROIDR
L7 13 S L4 AND THYROID
L8 0 S L4 AND ALOPECIA
L9 0 S L4 AND BALD?

FILE 'USPATFULL' ENTERED AT 16:08:23 ON 05 DEC 2003

L10 3 S L2

FILE 'CAPLUS, TOXCENTER' ENTERED AT 16:18:33 ON 05 DEC 2003

L11 2 FILE CAPLUS
L12 0 FILE TOXCENTER
TOTAL FOR ALL FILES
L13 2 S 40487-99-8/BIOL
L14 2 FILE CAPLUS
L15 0 FILE TOXCENTER

TOTAL FOR ALL FILES

L16 2 S 40487-99-8
L17 1 FILE CAPLUS
L18 0 FILE TOXCENTER

TOTAL FOR ALL FILES

L19 1 S 27486-96-0
L20 12 FILE CAPLUS
L21 1 FILE TOXCENTER

TOTAL FOR ALL FILES

L22 13 S 52050-08-5 OR 40487-99-8 OR L19
SAVE ALL L09980406/L

FILE 'CAPLUS, USPATFULL' ENTERED AT 16:23:42 ON 05 DEC 2003

L23 10 FILE CAPLUS
L24 8 FILE USPATFULL
TOTAL FOR ALL FILES
L25 18 S CARDIAC SPARING
L26 19 FILE CAPLUS
L27 35 FILE USPATFULL

TOTAL FOR ALL FILES

L28 54 S CARDIAC (5A) SPARING
L29 4 FILE CAPLUS
L30 5 FILE USPATFULL

TOTAL FOR ALL FILES

L31 9 S THYROID AND L28
L32 0 FILE CAPLUS
L33 0 FILE USPATFULL

TOTAL FOR ALL FILES

L34 0 S L22 AND L28
L35 0 FILE CAPLUS
L36 0 FILE USPATFULL

TOTAL FOR ALL FILES

L37 0 S L22 AND (CARDIAC)
L38 1 FILE CAPLUS
L39 0 FILE USPATFULL

TOTAL FOR ALL FILES

L40 1 S L22 AND (HEART OR PRESSURE)

FILE 'CAPLUS, TOXCENTER' ENTERED AT 16:39:26 ON 05 DEC 2003

L41 1 FILE CAPLUS

L42 0 FILE TOXCENTER

TOTAL FOR ALL FILES

L43 1 S L40

SAVE ALL L099804

L31 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

TI Effects of the novel **thyroid** hormone analogs, SKF L-94901, Dibit, and 3'-AC-T2 on mitochondrial function

AB The effects of L-T3 and three novel analogs, SKF L-94901 (3,5-dibromo-3'-pyridazinone-L-thyronine), Dibit (3,5-dibromo-3'-isopropyl-L-thyronine), and 3'-Ac-T2 (3'-acetyl-3,5-diiodo-L-thyronine), on mitochondrial parameters were detd. in hypothyroid rats. The parameters include the 24 h hormone-induced changes in the bcl complex and in the proton permeability of the mitochondrial inner membrane. The **cardiac sparing** analog, SKF L-94901, had no effect on mitochondrial respiration or proton permeability, but the analog did increase .alpha.-glycerophosphate dehydrogenase activity, mitochondrial ubiquinone content, and altered the bypass respiration in the bcl complex. Dibit also did not increase respiration significantly but did change the other parameters. 3'-Ac-T2 increased respiration, mitochondrial ubiquinone content, proton permeability, enzyme activity and altered the bypass of the antimycin A blockage in the bcl complex.

ST **thyroid** hormone analog mitochondria

IT Animal respiration
Electron transport system, biological
Mitochondria
(**thyroid** hormone analogs effect on mitochondrial function)

IT **Thyroid** hormones
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**thyroid** hormone analogs effect on mitochondrial function)

IT Ubiquinones
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**thyroid** hormone analogs effect on mitochondrial function)

IT 6893-02-3, Triiodothyronine 13724-85-1, Dibit 93800-43-2, 3'-Acetyl-3,5-diiodo-L-thyronine 105211-23-2, SKF L-94901
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**thyroid** hormone analogs effect on mitochondrial function)

IT 9027-03-6, Cytochrome bcl 9075-65-4, .alpha.-Glycerophosphate dehydrogenase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**thyroid** hormone analogs effect on mitochondrial function)

ACCESSION NUMBER: 1996:338854 CAPLUS

DOCUMENT NUMBER: 125:26674

TITLE: Effects of the novel **thyroid** hormone analogs, SKF L-94901, Dibit, and 3'-AC-T2 on mitochondrial function

AUTHOR(S): Horrum, Mark A.; Tobin, Richard B.; Ecklund, Robert E.

CORPORATE SOURCE: College Medicine, University Nebraska Medical Center, Omaha, NE, 68105, USA

SOURCE: Biochemistry and Molecular Biology International (1996), 38(1), 61-72
CODEN: BMBIES; ISSN: 1039-9712

PUBLISHER: Academic

DOCUMENT TYPE: Journal

LANGUAGE: English

L31 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

AB CGS 26214, a thyromimetic substance devoid of cardiovascular effects in rats and dogs, binds to rat liver nuclear L-T3 receptors with an IC50 of 0.1 nM vs. 0.6 nM for L-T3, and lowered serum cholesterol in hypercholesterolemic rats at 1 .mu.g/kg vs. 25 .mu.g/kg for L-T3. In normocholesterolemic dogs and monkeys, CGS 26214 lowered LDL-cholesterol by 59 and 20%, resp. at 1 .mu.g/kg p.o., CGS 26214 decreased Lp(a) by 42% in cynomolgus monkeys at 30 .mu.g/kg p.o., and enhanced postprandial

triglyceride clearance in rats. The **cardiac-sparing** activity is attributed to preferential uptake into hepatocyte nuclei vs. cardiac nuclei of intact cells.

IT **Thyroid** hormones

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antihypercholesteremic activity of)

ACCESSION NUMBER: 1995:831098 CAPLUS
DOCUMENT NUMBER: 123:306205
TITLE: CGS 26214, the thyroxine connection revisited
AUTHOR(S): Steele, R. E.; Wasvary, J. M.; Dardik, B. N.;
Schwartzkopf, C. D.; Sharif, R.; Leonards, K. S.; Hu,
C. W.; Yurachek, E. C.; Stephan, Z. F.
CORPORATE SOURCE: Research Department, Ciba-Geigy Corporation, Summit,
NJ, 07901, USA
SOURCE: International Congress Series (1995),
1066 (Atherosclerosis X), 321-4
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

L31 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

TI Synthesis of **thyroid** hormone analogs. Part 1. Preparation of
3'-heteroarylmethyl-3,5-diiodo-L-thyronines via phenol-dinitrophenol
condensation and relationships between structure and selective
thyromimetic activity

AB 3'-Heteroarylmethyl analogs, e.g. I (R = H, F), of the natural
thyroid hormone 3,3',5-triiodo-L-thyronine (T3) were synthesized
as potential selective (**cardiac-sparing**)
thyromimetics. The di-Ph ether moiety was constructed by condensation of
3-substituted 4-methoxyphenols with a 3,5-dinitro-L-tyrosine deriv.
Synthesis of the key phenols required the in situ prepn., at low temps.,
of novel metalated species, e.g. 2-lithio-5-methoxypyridine, and
2,6-difluoro-3-lithiopyridine, followed by reaction with
2,4-MeO(PhCH2O)C6H3CHO. Structure-activity relationships indicate that
selective thyromimetic activity is assocd. with 2-oxyheteroaren-5-ylmethyl
3'-substitution, as found in the pyridone I (R = H). The location of the
oxy substituent in the heterocycle is crit. for both hormonal activity and
for binding to the T3 receptor.

ST heteroarylmethyldiiodothyronine thyromimetic MSBAR; T3 heteroarylmethyl
analog **thyroid** hormone

IT **Thyroid** hormones

RL: RCT (Reactant); RACT (Reactant or reagent)
((heteroarylmethyl)diiodothyronines as)

ACCESSION NUMBER: 1989:173720 CAPLUS
DOCUMENT NUMBER: 110:173720
TITLE: Synthesis of **thyroid** hormone analogs. Part
1. Preparation of 3'-heteroarylmethyl-3,5-diiodo-L-
thyronines via phenol-dinitrophenol condensation and
relationships between structure and selective
thyromimetic activity
AUTHOR(S): Leeson, Paul D.; Emmett, John C.
CORPORATE SOURCE: Smith Kline and French Res. Ltd.,
Welwyn/Hertfordshire, AL6 9AR, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions
1: Organic and Bio-Organic Chemistry (1972-1999)
(1988), (12), 3085-96
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:173720

L31 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

TI Selective thyromimetics. **Cardiac-sparing**
thyroid hormone analogs containing 3'-arylmethyl substituents
AB Introduction of specific arylmethyl groups at the 3'-position of the
thyroid hormone 3,3',5'-triiodo-L-thyronine (T3), and its known
hormonally active derivs., gives liver-selective, **cardiac-**
sparing thyromimetics (e.g., I, X = O, S; R = aryl group), with
potential utility as plasma cholesterol lowering agents. Correlations
between in vivo and in vitro receptor binding affinities show that
liver/heart selectivity does not depend on receptor recognition but on
penetration or access to receptors in vivo. QSAR studies of the binding
data of a series of 20 3'-arylmethyl T3 analogs show that electroneg.
groups at the para position increase both receptor binding and selectivity
in vivo. However, increasing 3'-arylmethyl hydrophobicity increases
receptor binding but reduces selectivity. Substitution at ortho and meta
positions reduces both binding and selectivity. Replacement of the
3,5-iodo groups by halogen or Me maintains selectivity, with 3,5-dibromo
analogs in particular having increased potency combined with oral
bioavailability. Di-Ph thioether derivs. also have improved potency but
are less orally active. At the 1-position, the D enantiomer retains
selectivity, but removal of the .alpha.-amino to give a propionic acid
results in loss of selective thyromimetic activity.

IT **Thyroid** hormones

RL: RCT (Reactant); RACT (Reactant or reagent)
(arylmethyldiiodothyronines as)

ACCESSION NUMBER: 1989:115292 CAPLUS

DOCUMENT NUMBER: 110:115292

TITLE: Selective thyromimetics. **Cardiac-**

sparing thyroid hormone analogs
containing 3'-arylmethyl substituents

AUTHOR(S): Leeson, Paul D.; Emmett, John C.; Shah, Virendra P.;
Showell, Graham A.; Novelli, Ricardo; Prain, H.
Douglas; Benson, Martin G.; Ellis, David; Pearce,
Nigel J.; Underwood, Anthony H.

CORPORATE SOURCE: Smith Kline French Res. Ltd., Frythe/Welwyn, AL6 9AR,
UK

SOURCE: Journal of Medicinal Chemistry (1989), 32(2), 320-36
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 110:115292

L31 ANSWER 5 OF 9 USPATFULL on STN

SUMM Interestingly, it is known that the **thyroid** hormone known as
thyroxine ("T4") converts to thyronine ("T3") in human skin by
deiodinase I, a selenoprotein. Selenium deficiency causes a decrease in
T3 levels due to a decrease in deiodinase I activity; this reduction in
T3 levels is strongly associated with hair loss. Consistent with this
observation, hair growth is a reported side effect of administration of
T4. See, e.g., Berman, "Peripheral Effects of L-Thyroxine on Hair Growth
and Coloration in Cattle", Journal of Endocrinology, Vol. 20, pp.
282-292 (1960); and Gunaratnam, "The Effects of Thyroxine on Hair Growth
in the Dog", J. Small Anim. Pract., Vol. 27, pp. 17-29 (1986).
Furthermore, T3 and T4 have been the subject of several patent
publications relating to treatment of hair loss. See, e.g., Fischer et
al., DE 1,617,477, published Jan. 8, 1970; Mortimer, GB 2,138,286,
published Oct. 24, 1984; and Lindenbaum, WO 96/25943, assigned to Life
Medical Sciences, Inc., published Aug. 29, 1996.

SUMM Unfortunately, however, administration of T3 and/or T4 to treat hair
loss is not practicable because these **thyroid** hormones are
also known to induce significant cardiotoxicity. See, e.g., Walker et
al., U.S. Pat. No. 5,284,971, assigned to Syntex, issued Feb. 8, 1994
and Emmett et al., U.S. Pat. No. 5,061,798, assigned to Smith Kline &
French Laboratories, issued Oct. 29, 1991. Surprisingly, however, the

present inventors have discovered compounds which promote hair growth without inducing cardiotoxicity. Consistent with this discovery, but without intending to be limited by theory, the present inventors have surprisingly discovered that the compounds useful in the present invention interact strongly with hair-selective **thyroid** hormone receptors but interact less strongly, or not at all, with heart-selective hormone receptors. These unique properties are, of course, not shared with T3 and/or T4. Accordingly, the compounds described for use in the methods and compositions herein are **cardiac-sparing** compounds useful for treating hair loss, including arresting and/or reversing hair loss and promoting hair growth.

- SUMM The present invention relates to methods for treating hair loss comprising administering a **cardiac-sparing** compound which has been found by the present inventors to be particularly useful for treating hair loss in mammals, including arresting and/or reversing hair loss and promoting hair growth. The compounds utilized in the present method have the structure: ##STR2##
- SUMM In addition to discovering that the present compounds are useful for treating hair loss, the present inventors have also surprisingly discovered that the preferred compounds are **cardiac-sparing**. The preferred compounds useful in the method of the present invention are therefore, as defined herein below, **cardiac-sparing**.
- SUMM The present invention relates to methods of treating hair loss by administering a compound having a structure as described herein. Preferably, the compound utilized in the present invention will be **cardiac-sparing**. Compounds (test compounds) may be tested for their ability to induce anagen and their lack of cardiotoxicity (**cardiac-sparing**) using the following methods. Alternatively, other methods well-known in the art may be used (but with the term "**cardiac-sparing**" being defined according to the method disclosed herein below).
- SUMM The cardiotoxicity assay measures the potential of a test compound to adversely affect the cardiovascular system. As **thyroid** hormone (T3) damages the cardiovascular system, the heart enlarges. See, e.g., Gomberg-Maitland et al., "**Thyroid** hormone and Cardiovascular Disease", American Heart Journal, Vol. 135(2), pp. 187-196 (1998); Klein and Ojamaa, "**Thyroid** Hormone and the Cardiovascular System", Current Opinion in Endocrinology and Diabetes, Vol. 4, pp. 341-346 (1997); and Klemperer et al., "**Thyroid** Hormone Therapy and Cardiovascular Disease", Progress in Cardiovascular Diseases, Vol. 37 (4), pp. 329-336 (1996). This increases the weight of the heart relative to whole body weight. The cardiotoxicity assay herein below is used to test compounds for potentially adverse cardiac effects by measuring their effect on the heart-to-body weight ratio.
- SUMM The index C is then calculated by dividing RT by RV. As defined herein, where C is less than 1.3, the test compound is **cardiac-sparing**. Preferably, C is less than 1.2, more preferably less than 1.15, and most preferably less than 1.1. In accordance with this method, T3 and T4 are not **cardiac-sparing**.
- SUMM Preferably the compounds of the present invention are, as defined herein, **cardiac-sparing**.
- CLM What is claimed is:
1. A method of treating hair loss comprising administering a composition comprising a **cardiac-sparing** compound characterized by the structure: ##STR4## and pharmaceutically acceptable salts,

hydrates, and biohydrolyzable amides, esters, and imides thereof, wherein: R.sub.1 is --(CH.sub.2).sub.n(CHNR.sub.7R.sub.8).sub.mC(O)R.sub.9; n is an integer from 1 to 3; m is an integer from 0 to 1; R.sub.3 and R.sub.5 are each, independently, selected from the group consisting of chlorine, bromine, iodine, and --CH.sub.3; R.sub.7 and R.sub.8 are each, independently, selected from the group consisting of hydrogen and C.sub.1-C.sub.4 alkyl; R.sub.9 is selected from the group consisting of hydroxy, C.sub.1-C.sub.4 alkoxy, and --NR.sub.7R.sub.8; R.sub.31 is selected from the group consisting of hydrogen, chlorine, bromine, iodine, C.sub.1-C.sub.4 alkyl, C.sub.4-C.sub.6 cycloalkyl, C.sub.1-C.sub.4 haloalkyl, C.sub.4-C.sub.6 halocycloalkyl, and --CH(R.sub.10)Ar; Ar is selected from the group consisting of 5-hydroxypyrid-2-yl, 6-hydroxypyrid-3-yl, 6-hydroxypyridazin-3-yl, 6-methoxypyridazin-3-yl N-oxide, and 6-hydroxypyridazin-3-yl N-oxide; R.sub.10 is selected from the group consisting of hydrogen and C.sub.1-C.sub.4 alkyl; and R4, is selected from the group consisting of hydroxy and C.sub.1-C.sub.4 alkoxy.

ACCESSION NUMBER: 2003:296943 USPATFULL
 TITLE: Method of treating hair loss using sulfonyl
 thyromimetic compounds
 INVENTOR(S): Zhang, Lixin Lilly, Cincinnati, OH, United States
 Youngquist, Robert Scott, Mason, OH, United States
 PATENT ASSIGNEE(S): The University of Texas Southwestern Medical Center,
 Dallas, TX, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6646005 | B1 | 20031111 |
| | WO 2000072810 | | 20001207 |
| APPLICATION INFO.: | US 2002-980351 | | 20020221 (9) |
| | WO 2000-US5199 | | 20000301 |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1999-137023P | 19990601 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | GRANTED | |
| PRIMARY EXAMINER: | Spivack, Phyllis G. | |
| LEGAL REPRESENTATIVE: | Michael Best & Friedrich LLP | |
| NUMBER OF CLAIMS: | 8 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 0 Drawing Figure(s); 0 Drawing Page(s) | |
| LINE COUNT: | 1073 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L31 ANSWER 6 OF 9 USPATFULL on STN

AB The present disclosure describes methods for treating hair loss in mammals, including arresting and/or reversing hair loss and promoting hair growth. The methods comprise administering a **cardiac-sparing** compound having a structure of formula (I) as described herein and a pharmaceutically-acceptable carrier. ##STR1##

SUMM [0005] Interestingly, it is known that the **thyroid** hormone known as thyroxine ("T4") converts to thyronine ("T3") in human skin by deiodinase I, a selenoprotein. Selenium deficiency causes a decrease in T3 levels due to a decrease in deiodinase I activity; this reduction in T3 levels is strongly associated with hair loss. Consistent with this observation, hair growth is a reported side effect of administration of T4. See, e.g., Berman, "Peripheral Effects of L-Thyroxine on Hair Growth and Coloration in Cattle", Journal of Endocrinology, Vol. 20, pp. 282-292 (1960); and Gunaratnam, "The Effects of Thyroxine on Hair Growth in the Dog", J. Small Anim. Pract., Vol. 27, pp. 17-29 (1986). Furthermore, T3 and T4 have been the subject of several patent

publications relating to treatment of hair loss. See, e.g., Fischer et al., DE 1,617,477, published Jan. 8, 1970; Mortimer, GB 2,138,286, published Oct. 24, 1984; and Lindenbaum, WO 96/25943, assigned to Life Medical Sciences, Inc., published Aug. 29, 1996.

SUMM [0006] Unfortunately, however, administration of T3 and/or T4 to treat hair loss is not practicable because these **thyroid** hormones are also known to induce significant cardiotoxicity. See, e.g., Walker et al., U.S. Pat. No. 5,284,971, assigned to Syntex, issued Feb. 8, 1994 and Emmett et al., U.S. Pat. No. 5,061,798, assigned to Smith Kline & French Laboratories, issued Oct. 29, 1991. Surprisingly, however, the present inventors have discovered biphenyl derivatives which promote hair growth without inducing cardiotoxicity. Consistent with this discovery, but without intending to be limited by theory, the present inventors have surprisingly discovered that the biphenyl derivatives useful in the present invention interact strongly with hair-selective **thyroid** hormone receptors but interact less strongly, or not at all, with heart-selective hormone receptors. These unique properties are, of course, not shared with T3 and/or T4. Accordingly, the biphenyl derivatives described for use in the methods and compositions herein are **cardiac-sparing** compounds useful for treating hair loss, including arresting and/or reversing hair loss and promoting hair growth.

SUMM [0007] The present invention relates to methods for treating hair loss comprising administering a **cardiac-sparing** compound which has been found by the present inventors to be particularly useful for treating hair loss in mammals, including arresting and/or reversing hair loss and promoting hair growth. The compounds utilized in the present method are biphenyl derivatives having the structure: ##STR2##

SUMM [0010] In addition to discovering that the present compounds are useful for treating hair loss, the present inventors have also surprisingly discovered that the preferred compounds are **cardiac-sparing**. The preferred compounds useful in the method of the present invention are therefore, as defined herein below, **cardiac-sparing**.

SUMM [0080] The present invention relates to methods of treating hair loss by administering a compound having a structure as described herein. Preferably, the compound utilized in the present invention will be **cardiac-sparing**. Compounds (test compounds) may be tested for their ability to induce anagen and their lack of cardiotoxicity (**cardiac-sparing**) using the following methods. Alternatively, other methods well-known in the art may be used (but with the term "**cardiac-sparing**" being defined according to the method disclosed herein below).

SUMM [0082] The cardiotoxicity assay measures the potential of a test compound to adversely affect the cardiovascular system. As **thyroid** hormone (T3) damages the cardiovascular system, the heart enlarges. See, e.g., Gomberg-Maitland et al., "**Thyroid** hormone and Cardiovascular Disease", American Heart Journal, Vol. 135(2), pp. 187-196 (1998); Klein and Ojamaa, "**Thyroid** Hormone and the Cardiovascular System", Current Opinion in Endocrinology and Diabetes, Vol. 4, pp.341-346 (1997); and Klemperer et al., "**Thyroid** Hormone Therapy and Cardiovascular Disease", Progress in Cardiovascular Diseases, Vol. 37 (4), pp. 329-336 (1996). This increases the weight of the heart relative to whole body weight. The cardiotoxicity assay herein below is used to test compounds for potentially adverse cardiac effects by measuring their effect on the heart-to-body weight ratio.

SUMM [0092] The index C is then calculated by dividing RT by RV. As defined

herein, where C is less than 1.3, the test compound is **cardiac-sparing**. Preferably, C is less than 1.2, more preferably less than 1.15, and most preferably less than 1.1. In accordance with this method, T3 and T4 are not **cardiac-sparing**.

DETD [0124] Preferably the compounds of the present invention are, as defined herein, **cardiac-sparing**.

CLM What is claimed is:

1. A method of treating hair loss comprising administering a composition comprising a **cardiac-sparing** compound characterized by the structure: ##STR15## and pharmaceutically acceptable salts, hydrates, and biohydrolyzable amides, esters, and imides thereof, wherein: R is selected from the group consisting of hydrogen, hydroxy, esterified hydroxy, and etherified hydroxy; R.sub.1, R.sub.2, and R.sub.4 are each, independently, selected from the group consisting of hydrogen, halogen, trifluoromethyl and lower alkyl; R.sub.3 is selected from the group consisting of halogen, trifluoromethyl, lower alkyl, aryl, aryl-lower alkyl, cycloalkyl, cycloalkyl-lower alkyl, and: ##STR16## R.sub.8 is selected from the group consisting of hydrogen, lower alkyl, aryl, cycloalkyl, aryl-lower alkyl, and cycloalkyl-lower alkyl; R.sub.9 is selected from the group consisting of hydroxy and acyloxy; R.sub.10 is selected from the group consisting of hydrogen and lower alkyl; with the proviso that R.sub.9 and R.sub.10 collectively optionally represent oxo; W is selected from the group consisting of --O-- and --S--; X is selected from the group consisting of --NR.sub.7, S, and O; R.sub.5 is selected from the group consisting of hydrogen, lower alkyl, and aryl-lower alkyl and R.sub.6 is hydrogen; with the proviso that when X is --NR.sub.7, R.sub.5 and R.sub.6 together are optionally oxo; R.sub.7 is selected from the group consisting of hydrogen and lower alkyl; and Z is selected from the group consisting of carboxyl and carboxyl derivatized as a pharmaceutically acceptable ester or amide.

ACCESSION NUMBER: 2003:238573 USPATFULL
TITLE: Method of treating hair loss using diphenylether derivatives
INVENTOR(S): Zhang, Lixin Lilly, Cincinnati, OH, UNITED STATES
Youngquist, Robert Scott, Mason, OH, UNITED STATES
PATENT ASSIGNEE(S): The University of Texas Southwestern Medical Center, Dallas, TX (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|---------------|
| PATENT INFORMATION: | US 2003166731 | A1 | 20030904 |
| APPLICATION INFO.: | US 2003-373471 | A1 | 20030224 (10) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 2000-980408, filed on 8 Dec 2000, GRANTED, Pat. No. US 6525094 A 371 of International Ser. No. WO 2000-US5253, filed on 1 Mar 2000, PENDING | | |

| | NUMBER | DATE |
|--|---|---------------|
| PRIORITY INFORMATION: | US 1999-137022P | 19990601 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | MICHAEL BEST & FRIEDRICH, LLP, 100 E WISCONSIN AVENUE, MILWAUKEE, WI, 53202 | |
| NUMBER OF CLAIMS: | 10 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 1137 | |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. | | |

AB The present invention describes methods for treating hair loss in mammals, including arresting and/or reversing hair loss and promoting hair growth. The methods comprise administering a **cardiac-sparing** compound which is a derivative of diphenylether and pharmaceutically-acceptable carrier.

SUMM Interestingly, it is known that the **thyroid** hormone known as thyroxine ("T4") converts to thyronine ("T3") in human skin by deiodinase I, a selenoprotein. Selenium deficiency causes a decrease in T3 levels due to a decrease in deiodinase I activity; this reduction in T3 levels is strongly associated with hair loss. Consistent with this observation, hair growth is a reported side effect of administration of T4. See, e.g., Berman, "Peripheral Effects of L-Thyroxine on Hair Growth and Coloration in Cattle", Journal of Endocrinology, Vol. 20, pp. 282-292 (1960); and Gunaratnam, "The Effects of Thyroxine on Hair Growth in the Dog", J. Small Anim. Pract., Vol. 27, pp. 17-29 (1986). Furthermore, T3 and T4 have been the subject of several patent publications relating to treatment of hair loss. See, e.g., Fischer et al., DE 1,617,477, published Jan. 8, 1970; Mortimer, GB 2,138,286, published Oct. 24, 1984; and Lindenbaum, WO 96/25943, assigned to Life Medical Sciences, Inc., published Aug. 29, 1996.

SUMM Unfortunately, however, administration of T3 and/or T4 to treat hair loss is not practicable because these **thyroid** hormones are also known to induce significant cardiotoxicity. See, e.g., Walker et al., U.S. Pat. No. 5,284,971, assigned to Syntex, issued Feb. 8, 1994 and Emmett et al., U.S. Pat. No. 5,061,798, assigned to Smith Kline & French Laboratories, issued Oct. 29, 1991. Surprisingly, however, the present inventors have discovered biphenyl derivatives which promote hair growth without inducing cardiotoxicity. Consistent with this discovery, but without intending to be limited by theory, the present inventors have surprisingly discovered that the biphenyl derivatives useful in the present invention interact strongly with hair-selective **thyroid** hormone receptors but interact less strongly, or not at all, with heart-selective hormone receptors. These unique properties are, of course, not shared with T3 and/or T4. Accordingly, the biphenyl derivatives described for use in the methods and compositions herein are **cardiac-sparing** compounds useful for treating hair loss, including arresting and/or reversing hair loss and promoting hair growth.

SUMM The present invention relates to methods for treating hair loss comprising administering a **cardiac-sparing** compound which has been found by the present inventors to be particularly useful for treating hair loss in mammals, including arresting and/or reversing hair loss and promoting hair growth. The compounds utilized in the present method are biphenyl derivatives having the structure: ##STR1##

SUMM In addition to discovering that the present compounds are useful for treating hair loss, the present inventors have also surprisingly discovered that the preferred compounds are **cardiac-sparing**. The preferred compounds useful in the method of the present invention are therefore, as defined herein below, **cardiac-sparing**.

SUMM The present invention relates to methods of treating hair loss by administering a compound having a structure as described herein. Preferably, the compound utilized in the present invention will be **cardiac-sparing**. Compounds (test compounds) may be tested for their ability to induce anagen and their lack or cardiotoxicity (**cardiac-sparing**) using the following methods. Alternatively, other methods well-known in the art may be used (but with the term "**cardiac-sparing**" being defined according to the method disclosed herein below).

SUMM The cardiotoxicity assay measures the potential of a test compound to adversely affect the cardiovascular system. As **thyroid** hormone (T3) damages the cardiovascular system, the heart enlarges. See, e.g., Gomberg-Maitland et al., "**Thyroid** hormone and Cardiovascular Disease", American Heart Journal, Vol. 135(2), pp. 187-196 (1998); Klein and Ojamaa, "**Thyroid** Hormone and the Cardiovascular System", Current Opinion in Endocrinology and Diabetes, Vol. 4, pp.341-346 (1997); and Klemperer et al., "**Thyroid** Hormone Therapy and Cardiovascular Disease", Progress in Cardiovascular Diseases, Vol. 37 (4), pp. 329-336 (1996). This increases the weight of the heart relative to whole body weight. The cardiotoxicity assay herein below is used to test compounds for potentially adverse cardiac effects by measuring their effect on the heart-to-body weight ratio.

SUMM The index C is then calculated by dividing RT by RV. As defined herein, where C is less than 1.3, the test compound is **cardiac-sparing**. Preferably, C is less than 1.2, more preferably less than 1.15, and most preferably less than 1.1. In accordance with this method, T3 and T4 are not **cardiac-sparing**.

DETD Preferably the compounds of the present invention are, as defined herein, **cardiac-sparing**.

CLM What is claimed is:

1. A method of treating hair loss comprising administering a composition comprising a **cardiac-sparing** compound having the formula of: ##STR14## and pharmaceutically acceptable salts, hydrates, and biohydrolyzable amides, esters, and imides thereof, wherein: R is selected from the group consisting of hydrogen, hydroxy, esterified hydroxy, and etherified hydroxy; R.sub.1, R.sub.2, and R.sub.4 are each, independently, selected from the group consisting of hydrogen, halogen, trifluoromethyl and lower alkyl; R.sub.3 is selected from the group consisting of halogen, trifluoromethyl, lower alkyl, aryl, aryl-lower alkyl, cycloalkyl, cycloalkyl-lower alkyl, and: ##STR15## R.sub.8 is selected from the group consisting of hydrogen, lower alkyl, aryl, cycloalkyl, aryl-lower alkyl, and cycloalkyl-lower alkyl; R.sub.9 is selected from the group consisting of hydroxy and acyloxy; R.sub.10 is selected from the group consisting of hydrogen and lower alkyl; with the proviso that R.sub.9 and R.sub.10 collectively optionally represent oxo; W is selected from the group consisting of --O-- and --S--; X is selected from the group consisting of --NR.sub.7, S, and O; R.sub.5 is selected from the group consisting of hydrogen, lower alkyl, and aryl-lower alkyl and R.sub.6 is hydrogen; with the proviso that when X is --NR.sub.7, R.sub.5 and R.sub.6 together are optionally oxo; R.sub.7 is selected from the group consisting of hydrogen and lower alkyl; and Z is selected from the group consisting of carboxyl and carboxyl derivatized as a pharmaceutically acceptable ester or amide.

ACCESSION NUMBER: 2003:53830 USPATFULL
TITLE: Method of treating hair loss using diphenylether derivatives
INVENTOR(S): Zhang, Lixin Lilly, Cincinnati, OH, United States
Youngquist, Robert Scott, Mason, OH, United States
PATENT ASSIGNEE(S): The University of Texas Southwestern Medical Center,
Dallas, TX, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6525094 | B1 | 20030225 |
| | WO 2000072812 | | 20001207 |
| APPLICATION INFO.: | US 2000-980408 | | 20001208 (9) |
| | WO 2000-US5253 | | 20000301 |

| NUMBER | DATE |
|--------|------|
|--------|------|

PRIORITY INFORMATION: US 1999-137022P 19990601 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Criares, Theodore J.
LEGAL REPRESENTATIVE: Michael Best & Friedrich LLP
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1249
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L31 ANSWER 8 OF 9 USPATFULL on STN

SUMM [0006] Two naturally occurring **thyroid** hormones, namely, thyroxine or 3,5,3',5'-tetraiodo-L-thyronine (commonly referred to as "T.sub.4"), and thyronine or 3,5,3'-triiodo-L-thyronine (commonly referred to as "T.sub.3"), are shown below: ##STR1##

SUMM [0007] T.sub.3 is the more biologically active of the two and, as will be appreciated from the structural formulae provided above, differs from T.sub.4 by the absence of the 5' iodine. T.sub.3 may be produced directly from the **thyroid** gland or, in peripheral tissues, by the removal of the 5' iodine by deiodinase enzymes. Thyromimetic analogs are often designed to be structurally similar to T.sub.3. In addition, naturally occurring metabolites of T.sub.3 are known.

SUMM [0008] Interestingly, it is known that the **thyroid** hormone, thyroxine ("T.sub.4"), converts to triiodo-thyronine ("T.sub.3") in human skin by deiodinase I, a selenoprotein. Selenium deficiency causes a decrease in T.sub.3 levels due to a decrease in deiodinase I activity; this reduction in T.sub.3 levels is strongly associated with hair loss. Consistent with this observation, hair growth is a reported side effect of administration of T.sub.4. See, for example, Berman, "Peripheral Effects of L-Thyroxine on Hair Growth and Coloration in Cattle," Journal of Endocrinology, Vol. 20, pp. 282-292 (1960); and Gunaratnam, "The Effects of Thyroxine on Hair Growth in the Dog," J. Small Anim. Pract., Vol. 27, pp. 17-29 (1986). Furthermore, T.sub.3 and T.sub.4 have been the subject of several patent publications relating to treatment of hair loss. See, e.g., German patent 1,617,477; British patent 2,138,286; and WO 96/25943.

SUMM [0009] Thus, it is known that **thyroid** hormone can exert positive effects on hair growth; however, administration of T.sub.3 and/or T.sub.4 to treat hair loss is not practicable because these **thyroid** hormones are known to cause adverse side effects, such as inducing significant cardiotoxicity or adversely affecting bone mineral density and lean body mass. See, e.g., U.S. Pat. No. 5,284,971; and U.S. Pat. No. 5,061,798.

SUMM [0010] According to the present invention, it has been found that administration of certain thyromimetic compounds, as described below, which activate **thyroid** hormone receptors in certain tissues, including those in the hair follicle which control growth and hair production, but spare other tissues, such as the heart, could be used to increase hair growth in patients suffering from hair loss, or may be used to prevent or delay hair loss in patients just beginning to lose their hair.

SUMM [0012] Commonly assigned, published International patent application WO 00/51971 and commonly assigned, published European patent application EP 1 033 364 disclose certain oxamic acids and derivatives thereof as **thyroid** receptor ligands. Commonly assigned, published European Patent Application EP 1 088 819 discloses certain 6-azauracil derivatives as **thyroid** receptor ligands. Commonly assigned,

published European Patent Application EP 1 127 882 discloses certain tetrazole compounds as **thyroid** receptor ligands. Commonly assigned, published European Patent Application EP 1 148 054 discloses certain thiazolidinedione, oxadiazolidinedione and triazolone compounds, which are **thyroid** receptor ligands.

- SUMM [0013] The following are recent articles on **thyroid** hormone receptors (TRs): M. K. Ahsan et al., J. Med. Invest. 44: 179-184, 1998, studied the immunohistochemical localization of **thyroid** hormone receptors (TRs) in human scalp skin and concluded that the results demonstrated the presence of **thyroid** hormone nuclear receptors in human hair follicles. N. Billoni et al., British Journal of Dermatology 2000: 142: 645-652, established that TR.beta.1 was the predominant form of TR expressed in the human hair follicle. C. C. Thompson and M. C. Bottcher, Proc. Natl. Acad. Sci. USA, Vol. 94, pp. 8527-8532, August 1997, found that the product of a **thyroid** hormone-responsive gene, the lack of which confers a hairless phenotype, interacts with **thyroid** hormone receptors. A. G. Messenger, British Journal of Dermatology, 142, 631-635, 2000, discussed the relationship between **thyroid** hormone and hair growth.
- SUMM [0015] J. D. Safer, et al., **Thyroid** 11 (8): 717-24 (August 2001), found topical triiodothyronine stimulates epidermal proliferation, dermal thickening and hair growth in mice and rats.
- SUMM [0016] V. L. Malloy, et al., Abstract titled "Effect of Topically Applied **Thyroid** Hormone on Androgen Dependent Models of the Pilo-Sebaceous Apparatus," Clinical Research, Vol. 36, No. 5, page 814A (1998), observed an inhibitory effect on testosterone induced alopecia after treatment with topical T.sub.3 in the AGA mouse, a model for androgen dependent hair loss.
- SUMM [0019] More particularly, the present invention provides such methods wherein the compounds are **cardiac-sparing**.
- SUMM [0036] The preferred compounds useful in the methods of the present invention are **cardiac-sparing**. The term "**cardiac-sparing**" as used herein means that, at the dosages required for hair growth, the compounds useful in the methods of the present invention do not produce any observable cardiotoxicity in the mammal being treated.
- SUMM [0235] The ability of a thyromimetic compound to bind **thyroid** hormone receptors may be demonstrated in standard assays known in the art, such as the **Thyroid** Hormone Receptor Binding Assay, described at page 53 of published European application EP 1 088 819. Preferably, the thyromimetic compounds useful in the methods of the present invention are TR.beta.1-selective in the Binding Assay and, therefore, are more selective for the predominant form of the receptor present in human hair follicles, as recently stated in the art. As such, these compounds are expected to have a preferential effect on hair growth relative to cardiac endpoints and other undesirable endpoints.
- SUMM [0236] Also, as noted above, preferably, the compounds useful in the present invention are **cardiac-sparing**. Compounds may be tested for their **cardiac-sparing** properties using the following assay:
- SUMM [0237] As is well known by those skilled in the art, **thyroid** hormones affect cardiac functioning, for example, by causing an increase in the heart rate as well as an increase in tissue mass, or hypertrophy. The ability of the compounds useful in the methods of the present invention to cause the **thyroid** hormone-like, cardiotoxic effects may be demonstrated according to the following protocol:

CLM What is claimed is:
3. A method of claim 2 wherein the compound is **cardiac-sparing**.

12. A method of claim 11 wherein the compound is **cardiac-sparing**.

22. A method of claim 21 wherein the compound is **cardiac-sparing**.

31. A method of claim 30 wherein the compound is **cardiac-sparing**.

40. A method of claim 39 wherein the compound is **cardiac-sparing**.

ACCESSION NUMBER: 2003:10247 USPATFULL
TITLE: Method of treating hair loss using thyromimetic compounds
INVENTOR(S): Cornelius, Peter, Old Lyme, CT, UNITED STATES
 Doherty, Niall S., Stonington, CT, UNITED STATES
 Dow, Robert L., Waterford, CT, UNITED STATES
 Chiang, Yuan-Ching P., East Lyme, CT, UNITED STATES

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2003007941 | A1 | 20030109 |
| APPLICATION INFO.: | US 2002-160516 | A1 | 20020530 (10) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2001-294962P | 20010531 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | Pfizer Inc., Patent Department, MS8260-1611, Eastern Point Road, Groton, CT, 06340 | |
| NUMBER OF CLAIMS: | 57 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 2849 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L31 ANSWER 9 OF 9 USPATFULL on STN

AB R.sup.41 is OH or a bioprecursor thereof; and the pharmaceutically acceptable salts thereof; are structural analogs of the **thyroid** hormones T.sub.3 and T.sub.4 and exhibit selective thyromimetic activity. Pharmaceutical compositions of the novel compounds and their use for the treatment of mammalian cholesteremia are provided.

SUMM The natural **thyroid** hormones, 3, 3',5-triiodo-L-thyronine (T.sub.3) and L-thyroxine (T.sub.4), are recognized cholesteremics which, due to their potent effects on cardiac function, are not indicated for the therapeutic reduction of plasma cholesterol levels in euthyroid subjects.

SUMM Since Harington and Barger, Biochem. J. 21, 169-181 (1927), first reported the structure and synthesis of thyroxine, numerous studies have been conducted to identify and synthesize structural analogs which mimic the activity of the natural hormones. The comprehensive review by E. C. Jorgensen in Hormonal Proteins and Peptides, Li, C. H., Ed., Academic Press, New York, Vol. VI, Chapters 2 and 3, 57-204 (1978) summarizes the intensive efforts to vary the thyroxine substituent pattern to produce thyromimetics, primarily for **thyroid** replacement therapy.

SUMM Leeson, et al. have further reported that introduction of specific 3'-arylmethyl groups gives liver-selective, **cardiac-sparing** thyromimetics. Modifications to the 3,5-substituents, ether oxygen, and L-alanyl side chain were also disclosed. These authors observed that the ether oxygen may be replaced by sulfur or methylene, which maintain the orthogonal arrangement of the diphenyl aromatic rings. J. Med. Chem. 32, 320-336 (1989).

SUMM The compounds of this invention are structural analogs of T.sub.3 and T.sub.4 and exhibit selective thyromimetic activity. When tested in vivo, they mimic the cholesterol-lowering effects of the **thyroid** hormones, with little or no effect on the heart.

SUMM In addition, compounds of Formula (I) may be indicated in **thyroid** hormone replacement therapy in patients with compromised cardiac function.

ACCESSION NUMBER: 94:11538 USPATFULL
TITLE: 4-(3-cyclohexyl-4-hydroxy or-methoxy phenylsulfonyl)
3,5 dibromo phenyl acetic thyromimetic
cholesterol-lowering agents
INVENTOR(S): Walker, Keith A., Los Altos Hills, CA, United States
Labadie, Sharada S., Sunnyvale, CA, United States
Kertesz, Denis J., Mountain View, CA, United States
Laughton, Craig W., Palo Alto, CA, United States
PATENT ASSIGNEE(S): Syntex (U.S.A.) Inc., Palo Alto, CA, United States
(U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 5284971 | | 19940208 |
| APPLICATION INFO.: | US 1992-914837 | | 19920716 (7) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Daus, Donald G. | | |
| LEGAL REPRESENTATIVE: | Schmonsees, William, Lowin, David A., Krubiner, Alan M. | | |
| NUMBER OF CLAIMS: | 2 | | |
| EXEMPLARY CLAIM: | 1 | | |
| LINE COUNT: | 1027 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

EXAMINER'S CASE ACTION WORKSHEET

Application No.
09/778,154



Legal Instrument Examiner

CHECK TYPE OF ACTION

DATE OF COUNT

| | | |
|---|---|---|
| <input type="checkbox"/> Non-Final Rejection | <input type="checkbox"/> Restriction/Election Only | <input checked="" type="checkbox"/> Final Rejection |
| <input type="checkbox"/> Ex Parte Quayle | <input type="checkbox"/> Allowance | <input type="checkbox"/> Advisory Action |
| <input type="checkbox"/> Examiner's Answer | <input type="checkbox"/> Reply Brief Noted | <input type="checkbox"/> Non-Entry of Reply Brief |
| <input type="checkbox"/> Defective Notice of Appeal | <input type="checkbox"/> Interference Disposal SPE _____ (Approval for Disposal) | <input type="checkbox"/> Suspension (Examiner-Initiated) SPE _____ (initial) |
| <input type="checkbox"/> Defective Appeal Brief | <input type="checkbox"/> SIR Disposal (use only after FAOM) | <input type="checkbox"/> Supplemental Examiner's Amendment |
| <input type="checkbox"/> Miscellaneous Office Letter (With Shortened Statutory Period Set) | <input type="checkbox"/> Notice of Non-Responsive Amendment (With One Month Time Period set) | <input type="checkbox"/> Miscellaneous Office Letter (No Response Period Set) |
| <input type="checkbox"/> Abandonment after BPAI Decision | <input type="checkbox"/> Supplemental Action (excluding Examiner's Answer) | <input type="checkbox"/> Response to Rule 312 Amendment |
| <input type="checkbox"/> Letter Restarting Period for Response (e.g., Missing References) | <input type="checkbox"/> Interview Summary | <input type="checkbox"/> Authorization to Change Previous Office Action SPE: _____ (Initial) |
| <input type="checkbox"/> Abandonment | <input type="checkbox"/> Express Abandonment Date: _____ | <input type="checkbox"/> Other Specify: _____ |

Examiner's Name: Vickie Kim

AU: 1614

DETD Thyroxine analogues such as DIME have been described in the literature. However, unlike thyroxine, DIME was reported to have no significant metabolic or cell differentiating activity (as determined by tadpole metamorphosis) (Money et al., 1958, "The Effect of Change in Chemical Structure of Some Thyroxine Analogues on the Metamorphosis of Rana Pipiens Tadpoles," Endocrinology 3:20-28; Stasilli et al., 1959, "Antigoitrogenic and Calorigenic Activities of Thyroxine Analogues in Rats," Endocrinology 64:62-82). For example, uptake of iodine into the thyroid of rats is only marginally (15%) inhibited by DIME as compared to thyroxine (Money et al., 1959, "The Effect of Various Thyroxine Analogues on Suppression of Iodine-131 Uptake by the Rat Thyroid," Endocrinology 64:123-125). Furthermore, DIME was reported to have no inhibitory activity against the growth of a non-malignant mouse pituitary adenoma (Kumaoka et al., 1960, "The Effect of Thyroxine Analogues on a Transplantable Mouse Pituitary Tumor," Endocrinology 66:32-38; Grinberg et al., 1962, "Studies with Mouse Pituitary Thyrotropic Tumors. V. Effect of Various Thyroxine Analogs on Growth and Secretion," Cancer Research 22:835-841). No studies with malignant cells have been reported.

ACCESSION NUMBER: 1998:36781 USPATFULL
 TITLE: Method of treating malignant tumors with thyroxine analogues having no significant hormonal activity
 INVENTOR(S): Kun, Ernest, Mill Valley, CA, United States
 Mendeleyev, Jerome, Tiburon, CA, United States
 PATENT ASSIGNEE(S): Octamer, Inc., Mill Valley, CA, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|-----------------------------------|------|--------------|
| PATENT INFORMATION: | US 5736576 | | 19980407 |
| APPLICATION INFO.: | US 1996-655267 | | 19960604 (8) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Chang, Ceila | | |
| LEGAL REPRESENTATIVE: | Halluin, Albert P. Howrey & Simon | | |
| NUMBER OF CLAIMS: | 3 | | |
| EXEMPLARY CLAIM: | 1 | | |
| LINE COUNT: | 1365 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L18 ANSWER 30 OF 32 USPATFULL on STN

SUMM Another suitable class of optional **activity** enhancers are **thyroid hormones** and derivatives and analogs thereof. Examples of suitable **thyroid hormones** for use herein may include triiodothyronine. Examples of **thyroid hormone** analogs which may be suitable for use herein include those described in U.S. Provisional Patent Application No. 60/136,996, Zhang et al., "Method of Treating **Hair** Loss", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,024, Zhang et al., "Method of Treating **Hair** Loss Using Biphenyl Compounds", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,022, Zhang et al., "Method of Treating **Hair** Loss Using Carboxyl Derivatives", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,023, Zhang et al., "Method of Treating **Hair** Loss Using Sulfonyl Thyromimetic Compounds", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,052, Youngquist et al., "Biaryl Compounds", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,063, Youngquist et al., "Sulfur-Bridged Compounds", filed Jun. 1, 1999, and U.S. Provisional Patent Application No. 60/136,958, Youngquist et al., "Substituted Biaryl Ether Compounds", filed Jun. 1, 1999.

PI US 6124362

20000926

L18 ANSWER 30 OF 32 USPATFULL on STN

SUMM Another suitable class of optional **activity** enhancers are **thyroid hormones** and derivatives and analogs thereof. Examples of suitable **thyroid hormones** for use herein may include triiodothyronine. Examples of **thyroid hormone** analogs which may be suitable for use herein include those described in U.S. Provisional Patent Application No. 60/136,996, Zhang et al., "Method of Treating **Hair** Loss", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,024, Zhang et al., "Method of Treating **Hair** Loss Using Biphenyl Compounds", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,022, Zhang et al., "Method of Treating **Hair** Loss Using Carboxyl Derivatives", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,023, Zhang et al., "Method of Treating **Hair** Loss Using Sulfonyl Thyromimetic Compounds", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,052, Youngquist et al., "Biaryl Compounds", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,063, Youngquist et al., "Sulfur-Bridged Compounds", filed Jun. 1, 1999, and U.S. Provisional Patent Application No. 60/136,958, Youngquist et al., "Substituted Biaryl Ether Compounds", filed Jun. 1, 1999.

PI US 6124362

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L18 ANSWER 26 OF 32 USPATFULL on STN

DRWD Biological functions or **activities** of Hairless include, but are not limited to, transcription, growth and maintenance of **hair**, resistance to UV radiation and chemical-induced skin carcinogenesis, neural development, neurological or behavioral characteristics, and other effects of **thyroid hormone** mediated through Hairless.

DRWD In such embodiments of the invention, a method is provided for screening candidate chemical agents for the ability to modulate **hair** development and/or cell differentiation by activating HR-regulated gene expression or by inhibiting HR-regulated gene expression. Moreover, a method is provided for screening candidate chemical agents for use in modulating maintenance and/or growth of **hair**. Furthermore, a method of screening candidate chemical agents which modulate the binding of Hr to **thyroid hormone** receptor is provided to regulate hairless transcriptional **activity**. A high-throughput screening assay is preferred.

ACCESSION NUMBER: 2002:34327 USPATFULL

TITLE: Human hairless gene and protein

INVENTOR(S): Thompson, Catherine C., Baltimore, MD, United States

PATENT ASSIGNEE(S): The Carnegie Institution of Washington, Washington, DC, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6348348 | B1 | 20020219 |
| APPLICATION INFO.: | US 1999-287354 | | 19990407 (9) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1998-80888P | 19980407 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | GRANTED | |
| PRIMARY EXAMINER: | Carlson, Karen Cochrane | |
| LEGAL REPRESENTATIVE: | Pillsbury Winthrop LLP | |
| NUMBER OF CLAIMS: | 19 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 13 Drawing Figure(s); 13 Drawing Page(s) | |
| LINE COUNT: | 2650 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 27 OF 32 USPATFULL on STN

SUMM [0005] The **thyroid hormone** thyroxine ("T4") converts to thyronine ("T3") in human skin by deiodinase I, a selenoprotein. Selenium deficiency causes a decrease in T3 levels due to a decrease in deiodinase I **activity**; this reduction in T3 levels is strongly associated with **hair** loss. Consistent with this observation, **hair** growth is a reported side effect of administration of T4. See, e.g., Berman, "Peripheral Effects of L-Thyroxine on **Hair** Growth and Coloration in Cattle", Journal of Endocrinology, Vol. 20, pp. 282-292, (1960); and Gunaratnam, "The Effects of Thyroxine on **Hair** Growth in the Dog", J. Small Anim. Pract., Vol. 27, pp. 17-29 (1986). Furthermore, T3 and T4 have been the subject of several patent publications relating to treatment of **hair** loss. See, e.g., Fischer et al., DE 1,617,477, published Jan. 8, 1970; Mortimer, GB 2,138,286, published Oct. 24, 1984; and Lindenbaum, WO 96/25943, assigned to Life Medical Sciences, Inc., published Aug. 29, 1996.

ACCESSION NUMBER: 2002:22458 USPATFULL

TITLE: Cosmetic and pharmaceutical compositions and methods using 2-decarboxy-2-phosphinico derivatives

INVENTOR(S): DeLong, Mitchell Anthony, West Chester, OH, UNITED STATES

McIver, John McMillan, Cincinnati, OH, UNITED STATES
Youngquist, Robert Scott, Mason, OH, UNITED STATES

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 2002013294 | A1 | 20020131 |
| APPLICATION INFO.: | US 2001-774558 | A1 | 20010131 (9) |

| | NUMBER | DATE |
|--|--|---------------|
| PRIORITY INFORMATION: | US 2000-193845P | 20000331 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | THE PROCTER & GAMBLE COMPANY, PATENT DIVISION, IVORYDALE TECHNICAL CENTER - BOX 474, 5299 SPRING GROVE AVENUE, CINCINNATI, OH, 45217 | |
| NUMBER OF CLAIMS: | 30 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 1847 | |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. | | |

L18 ANSWER 28 OF 32 USPATFULL on STN

SUMM [0035] As is well known in the art, **hair** growth occurs by a cycle of **activity** which involves alternating periods of growth and rest. This cycle is often divided into three main stages which are known as anagen, catagen and telogen. Anagen is the growth phase of the cycle and may be characterized by penetration of the **hair** follicle deep into the dermis with rapid proliferation of cells, which are differentiating to form **hair**. The next phase is catagen, which is a transitional stage marked by the cessation of cell division, and during which the **hair** follicle regresses through the dermis and **hair** growth is ceased. The next phase, telogen, is often characterized as the resting stage during which the regressed follicle contains a germ with tightly packed dermal papilla cells. At telogen, the initiation of a new anagen phase is caused by rapid cell proliferation in the germ, expansion of the dermal papilla, and elaboration of basement membrane components. When **hair** growth ceases, most of the **hair** follicles reside in telogen and anagen is not engaged, thus causing the onset of full or partial **hair loss**. Interestingly, it is known that the **thyroid hormone** known as thyroxine ("T4") converts to thyronine ("T3") in human skin by deiodinase 1, a selenoprotein. Selenium deficiency causes a decrease in T3 levels due to a decrease in deiodinase I **activity**; this reduction in T3 levels is strongly associated with **hair** loss. Consistent with this observation, **hair** growth is a reported side effect of administration of T4. Furthermore, T3 and T4 have been the subject of several patent publications relating to treatment of **hair** loss, including, for example, International Patent Application Publication No. WO 00/72810, published Dec. 7, 2000; International Patent Application Publication No. WO 00/72811, published Dec. 7, 2000; International Patent Application Publication No. WO 00/72812, published Dec. 7, 2000; International Patent Application Publication No. WO 00/72813, published Dec. 7, 2000; International Patent Application Publication No. WO 00/72920, published Dec. 7, 2000; and International Patent Application Publication No. WO 00/73292, published Dec. 7, 2000; and references cited therein.

ACCESSION NUMBER: 2001:229704 USPATFULL
TITLE: Malonamic acids and derivatives thereof as thyroid receptor ligands
INVENTOR(S): Chiang, Yuan-Ching P., East Lyme, CT, United States
Aspnes, Gary E., Rockville, RI, United States
Estep, Kimberly G., Groton, CT, United States

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 2001051657 | A1 | 20011213 |
| | US 6664291 | B2 | 20031216 |
| APPLICATION INFO.: | US 2001-819283 | A1 | 20010328 (9) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2000-193618P | 20000331 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | Gregg C. Benson, Pfizer Inc., Patent Department, MS 4159, Eastern Point Road, Groton, CT, 06340 | |
| NUMBER OF CLAIMS: | 71 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 6251 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 29 OF 32 USPATFULL on STN

SUMM If the patient's **hair** loss is due to hypothyroidism, then increased **thyroid hormones** can be administered. If perceived **hair** loss is due to hyperthyroidism, then the patient's thyroid **activity** can be reduced by drug therapy. It is noted that hypothyroidism diminishes the amount of **hair** that will grow because of decreased metabolic rates. Hyperthyroidism causes **hairs** to become very fine, and the very fine **hairs** are perceived to be **hair** loss.

ACCESSION NUMBER: 2001:22261 USPATFULL
 TITLE: Methods and compositions for the promotion of hair growth
 INVENTOR(S): Hallam, Kenneth M., 9609 Labrador La., Cockeysville, MD, United States 21030
 Robinson, Howard N., 18 Hickory Knoll Ct., Lutherville, MD, United States 21093

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 6187815 | B1 | 20010213 |
| APPLICATION INFO.: | US 1996-608954 | | 19960229 (8) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1994-315903, filed on 30 Sep 1994, now abandoned Continuation-in-part of Ser. No. US 1992-837222, filed on 18 Feb 1992, now abandoned | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Moezie, Minna | | |
| ASSISTANT EXAMINER: | Wang, S. | | |
| LEGAL REPRESENTATIVE: | Bloom, Leonard | | |
| NUMBER OF CLAIMS: | 4 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 1 Drawing Figure(s); 1 Drawing Page(s) | | |
| LINE COUNT: | 1236 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 30 OF 32 USPATFULL on STN

SUMM Another suitable class of optional **activity** enhancers are **thyroid hormones** and derivatives and analogs thereof. Examples of suitable **thyroid hormones** for use herein may include triiodothyronine. Examples of **thyroid hormone** analogs which may be suitable for use herein include those described in U.S. Provisional Patent Application No. 60/136,996, Zhang et al., "Method of Treating **Hair** Loss", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,024, Zhang et al., "Method of Treating **Hair** Loss Using Biphenyl Compounds", filed

Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,022, Zhang et al., "Method of Treating Hair Loss Using Carboxyl Derivatives", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,023, Zhang et al., "Method of Treating Hair Loss Using Sulfonyl Thyromimetic Compounds", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,052, Youngquist et al., "Biaryl Compounds", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,063, Youngquist et al., "Sulfur-Bridged Compounds", filed Jun. 1, 1999, and U.S. Provisional Patent Application No. 60/136,958, Youngquist et al., "Substituted Biaryl Ether Compounds", filed Jun. 1, 1999.

ACCESSION NUMBER: 2000:128394 USPATFULL
 TITLE: Method for regulating hair growth
 INVENTOR(S): Bradbury, Barton James, West Chester, OH, United States
 Soper, Shari Joy, Cincinnati, OH, United States
 Kaczvinsky, Jr., Joseph Robert, Cincinnati, OH, United States
 Bailey, Dorothy Limerick, Fairfield, OH, United States
 Gale, Celeste Dawn, Hamilton, OH, United States
 PATENT ASSIGNEE(S): The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6124362 | | 20000926 |
| APPLICATION INFO.: | US 1999-353408 | | 19990715 (9) |

| | NUMBER | DATE |
|-----------------------|-----------------|---------------|
| PRIORITY INFORMATION: | US 1998-93285P | 19980717 (60) |
| | US 1999-122925P | 19990305 (60) |
| | US 1998-102449P | 19980930 (60) |
| | US 1998-102448P | 19980930 (60) |
| | US 1998-102539P | 19980930 (60) |
| | US 1998-102458P | 19980930 (60) |
| | US 1998-102437P | 19980930 (60) |
| | US 1999-136996P | 19990601 (60) |
| | US 1999-137024P | 19990601 (60) |
| | US 1999-137022P | 19990601 (60) |
| | US 1999-137023P | 19990601 (60) |
| | US 1999-137052P | 19990601 (60) |
| | US 1999-137063P | 19990601 (60) |
| | US 1999-136958P | 19990601 (60) |

DOCUMENT TYPE: Utility
 FILE SEGMENT: Granted
 PRIMARY EXAMINER: Jarvis, William R.A.
 ASSISTANT EXAMINER: Kim, Vickie
 LEGAL REPRESENTATIVE: Rosnell, Tara M., Hilton, Michael E., Rasser, Jacobus C.

NUMBER OF CLAIMS: 10
 EXEMPLARY CLAIM: 1
 LINE COUNT: 1662
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 31 OF 32 USPATFULL on STN

DETD The present invention recognizes that **thyroid hormones** and STHs can directly modulate GAG production or HA secretion from cells, such as trabecular meshwork cells. Methods of the invention, consequently, are directed to modulating GAG production or HA secretion using compounds, especially STHs, that reduce the amount or **activity** of such substances or cellular processes in the desired cells or tissues. Preferably, such cells will be trabecular meshwork cells, ciliary cells of the eye, endothelial cells of the eye, non-eye

endothelial cells, **hair** follicles and fibroblasts of skin and internal organs. In most instances non-systemic application of a STH is preferred, although STHs can be administered systemically as well.

ACCESSION NUMBER: 2000:50735 USPATFULL
TITLE: Eye treatments using synthetic thyroid hormone compositions
INVENTOR(S): Schwartz, Daniel M., San Francisco, CA, United States
Baxter, John D., San Francisco, CA, United States
Jumper, Michele D., SF, CA, United States
Scanlan, Thomas S., San Francisco, CA, United States
PATENT ASSIGNEE(S): Regents of the University of California, Oakland, CA, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6054485 | | 20000425 |
| APPLICATION INFO.: | US 1997-915232 | | 19970820 (8) |

| | NUMBER | DATE |
|-----------------------|---|---------------|
| PRIORITY INFORMATION: | US 1996-23697P | 19960820 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | Granted | |
| PRIMARY EXAMINER: | Witz, Jean C. | |
| LEGAL REPRESENTATIVE: | Cooley Godward LLP | |
| NUMBER OF CLAIMS: | 12 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 10 Drawing Figure(s); 6 Drawing Page(s) | |
| LINE COUNT: | 1799 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 32 OF 32 USPATFULL on STN

SUMM The effects of androgens in MPB are mediated by the binding of an androgen (primarily DHT) to the androgen receptor (AR). Androgens bind specifically to the AR, which is either situated in the nucleus or transferred to it from the cytoplasm. The AR belongs to a subfamily of steroid/**thyroid hormone**/retinoic acid receptors, whose **activity** is controlled by the tight and specific binding of the cognate ligand. Evidence for the involvement of the AR in MPB includes the demonstration that androgenic **alopecia** (a type of pattern **baldness** in women) can be alleviated by treatment with antiandrogens. These antiandrogens, such as spironolactone, cyproterone acetate, flutamide and cimetidine, bind to the AR and competitively inhibit DHT binding. In addition, sebaceous glands of **bald** scalps were found to have greater binding affinity and capacity for androgens than those in hairy scalps.

ACCESSION NUMBER: 1999:27619 USPATFULL
TITLE: Compositions and methods of treatment of androgen-associated baldness using antisense oligomers
INVENTOR(S): Harper, Mary Ellen, Carlsbad, CA, United States
Woolf, Tod Mitchell, Del Mar, CA, United States
Arnold, Jr., Lyle John, Poway, CA, United States
PATENT ASSIGNEE(S): Genta Incorporated, San Diego, CA, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 5877160 | | 19990302 |
| APPLICATION INFO.: | US 1995-483464 | | 19950607 (8) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 1994-308170, filed on 16 Sep 1994, now abandoned which is a continuation of Ser. No. US 1993-19543, filed on 19 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. | | |

US 1991-707879, filed on 31 May 1991, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Marschel, Ardin H.
LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear, LLP
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 1416
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L18 ANSWER 22 OF 32 USPATFULL on STN

SUMM Another suitable class of optional **activity** enhancers are **thyroid hormones** and derivatives and analogs thereof. Examples of suitable **thyroid hormones** for use herein may include triiodothyronine. Examples of **thyroid hormone** analogs which may be suitable for use herein include those described in U.S. Provisional Patent Application No. 60/136,996, Zhang et al., "Method of Treating **Hair** Loss", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,024, Zhang et al., "Method of Treating **Hair** Loss Using Biphenyl Compounds", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,022, Zhang et al., "Method of Treating **Hair** Loss Using Carboxyl Derivatives", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,023, Zhang et al., "Method of Treating **Hair** Loss Using Sulfonyl Thyromimetic Compounds", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,052, Youngquist et al., "Biaryl Compounds", filed Jun. 1, 1999, U.S. Provisional Patent Application No. 60/137,063, Youngquist et al., "Sulfur-Bridged Compounds", filed Jun. 1, 1999, and U.S. Provisional Patent Application No. 60/136,958, Youngquist et al., "Substituted Biaryl Ether Compounds", filed Jun. 1, 1999.

ACCESSION NUMBER: 2002:239002 USPATFULL
TITLE: Method for regulating hair growth
INVENTOR(S): Bradbury, Barton James, West Chester, OH, United States
Soper, Shari Joy, Cincinnati, OH, United States
Kaczvinsky, Jr., Joseph Robert, Cincinnati, OH, United States
Bailey, Dorothy Limerick, Fairfield, OH, United States
Gale, Celeste Dawn, Hamilton, OH, United States
PATENT ASSIGNEE(S): The University of Texas Southwestern Medical Center,
Dallas, TX, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 6451777 | B1 | 20020917 |
| APPLICATION INFO.: | US 2000-567738 | | 20000510 (9) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1999-353408, filed on 15 Jul 1999, now patented, Pat. No. US 6124362 | | |

| | NUMBER | DATE |
|--|--|---------------|
| PRIORITY INFORMATION: | US 1998-93285P | 19980717 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | GRANTED | |
| PRIMARY EXAMINER: | Jarvis, William R. A. | |
| ASSISTANT EXAMINER: | Kim, Vickie Y. | |
| LEGAL REPRESENTATIVE: | Michael Best & Friedrich LLP | |
| NUMBER OF CLAIMS: | 12 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 0 Drawing Figure(s); 0 Drawing Page(s) | |
| LINE COUNT: | 1702 | |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. | | |